Central Asian Journal of Medical Sciences
CAJMS

Case Report

Cent Asian J Med Sci. 2020 March;6(1):379-383. https://doi.org/10.24079/CAJMS.2020.03.007

A Case of Osler-Weber-Rendu Syndrome Complicated with Nasal Septum Perforation

Odgerel Tsogbadrakh[1,2], Injinaash Ogoosambuu[1], Layla Jukhai[2], Munkhbaatar Davasumberel[2], Khatanbaatar Alexandr.[3]

[1] Department of Hematology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [2] Mongol-Japan Teaching Hospital, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [3] Khatagtai Hospital, Ulaanbaatar, Mongolia

Submitted: February 16, 2020
Revised: February 26, 2020
Accepted: March 3, 2020

Corresponding Author
Odgerel Tsogbadrakh
Department of Hematology, School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia
Tel: + 976-99505725
E-mail: odgerel.ts@mnums.edu.mn

Objectives: Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease) is a rare autosomal dominant disorder characterized by multiple mucocutaneous telangiectasias and visceral arteriovenous malformations. We report the first case of Randu-Osler-Weber disease complicated with nasal septum perforation. **Method:** Diagnosis was based on physical examination and genetic testing. **Results:** A 52 years old female presented to the Mongol-Japan Teaching Hospital for evaluation of anemia and recurrent epistaxis. On physical examination, telangiectasias were found on eye mucous, tongue tip, palms, and fingers. An ACVRL 1 mutation was detected by genetic testing. **Conclusion:** On the basis of clinical features in this patient telangiectatic lesions in nasal cavity lead to epistaxis which is more common than mucocutaneous telangiectasia in HTT. Recurrent nose bleeding leads to iron deficiency anemia.

Keyword: Hereditary hemorrhagic telangiectasia, arteriovenous malformations, epistaxis, iron deficiency, ACVRL1 gene mutation

Introduction

Hereditary hemorrhagic telangiectasia (HHT) also known as Osler-Weber-Rendu disease (OWRD), is an autosomal dominant disorder characterized by multiple mucocutaneous telangiectasias and arteriovenous malformations (AVMs) in visceral organs [1]. The prevalence of this disorder is 1 to 2 cases per 10,000 population. HTT has a higher prevalee in certain populations such as the Afro-Caribbean residents of Curacao and Bonaire due to hereditary variables [2].

Multiple telangiectasias on the face, lips, oral cavity, nose and finger are common. Spontaneous epistaxis is noted in more than 90% of patients with HTT [3]. Multiple intrahepatic AVMs presented in 40-50% of HTT patients [2]. The severity and frequency of epistaxis generally increase with age and more than half of HHT patients develop iron deficiency anemia due to recurrent blood loss [4].

Curacao criteria is a widely accepted standard for the

diagnosis of HHT [5]. An individual is considered to have HHT if three of the following diagnosing criteria are met; recurrent spontaneous epistaxis, mucocutaneous telangiectasia, visceral involvement such as pulmonary, cerebral spinal AVMs, gastrointestinal bleeding intrahepatic shunting, and family history of HHT. The presence of two criteria warrants a possible or suspected diagnosis [3-6].

More than 80% of HHT patients have identifiable mutations [7]. Endoglin (ENG), activin receptor type II-like1 (ACVRL1/ALK1), and SMAD4 mutations cause HHT1, HHT2, and Juvenile Polyposis HTT (JP/HHT) respectively [8-10]. Genetic changes are well associated with phenotypes in HHT. Pulmonary and cerebral AVMs have been shown more common in patients with HHT1 than with HHT2, whereas intrahepatic vascular malformations are more common in patients with HHT2 than HHT1 [11,12]. Also, the rate of AVMs is less well known in JP/HHT patients [13].

Only one case of possible HHT has been described previously in Mongolia in the 1990s [14]. Because of the variability of clinical symptoms and rarity, the diagnose of HHT is often delayed. Diagnose and management of HHT are challenging in Mongolia.

Case report

A 52 years old female came to the outpatient clinic of Mongol-Japan Teaching hospital with complaints of recurrent epistaxis, fatigue and tiredness. She had an episode of bleeding during gastroscopy 3 years ago. On physical examination many telangiectasias were found on eye mucous, lip vermilions, tongue tip, palms, and fingers all of which suggested the diagnosis of Randu-Osler-Weber syndrome (Figure 1A, B, C). Endoscopy revealed telangiectatic lesions were distributed on the mucosal surface from the pharynx to the duodenum, on the tongue, and palate (Figure 1D, E, F). CBC showed mild hypochromic microcytic anemia (Hb 11.2 g/dl, MCV 78fl, MCH23 pg). The liver function and coagulation tests were normal.

CT angiography is frequently necessary for revealing of visceral AVMs. CT angiography of the liver of the patient showed an

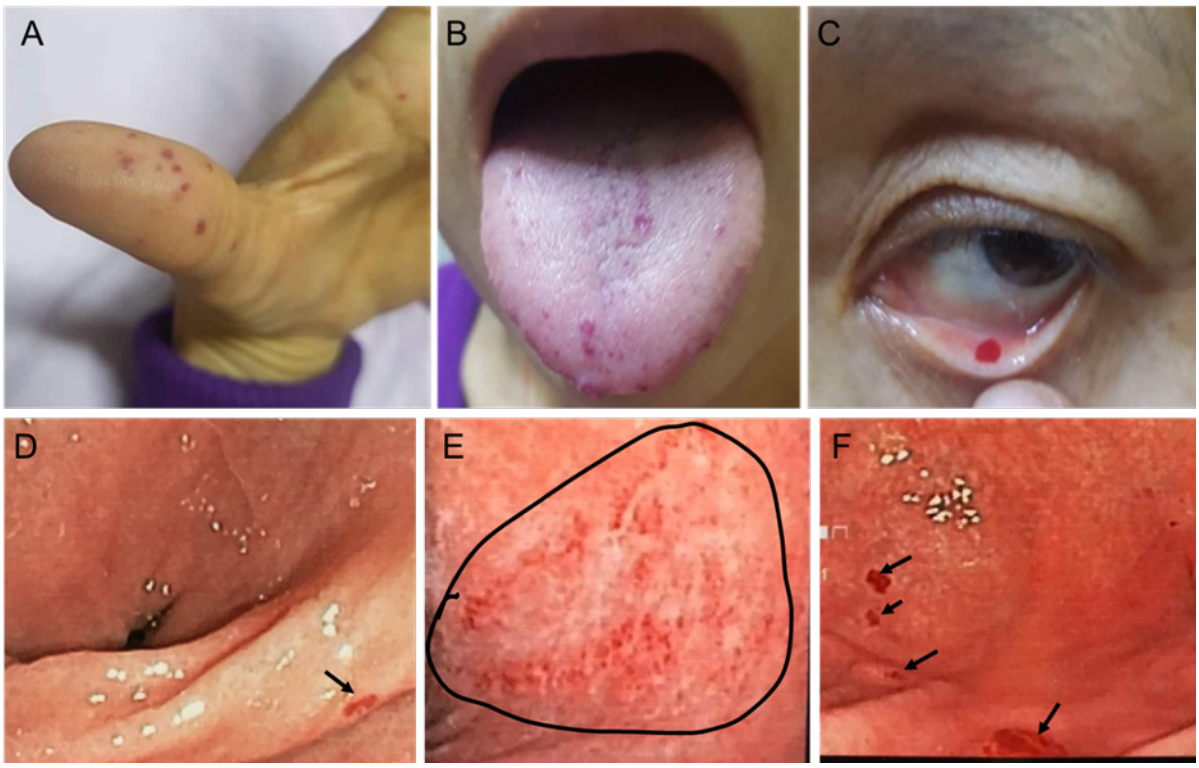

Figure 1. Clinical features of the patient with HHT. Mucocutaneous telangiectasia was seen by physical examination: over the tips of fingers (A), tongue (B), and eye (C) mucoses. Endoscopic images showed multiple angiodysplasias (arrows) in the oral mucosa, gastric corpus, and duodenum (D, E, F).

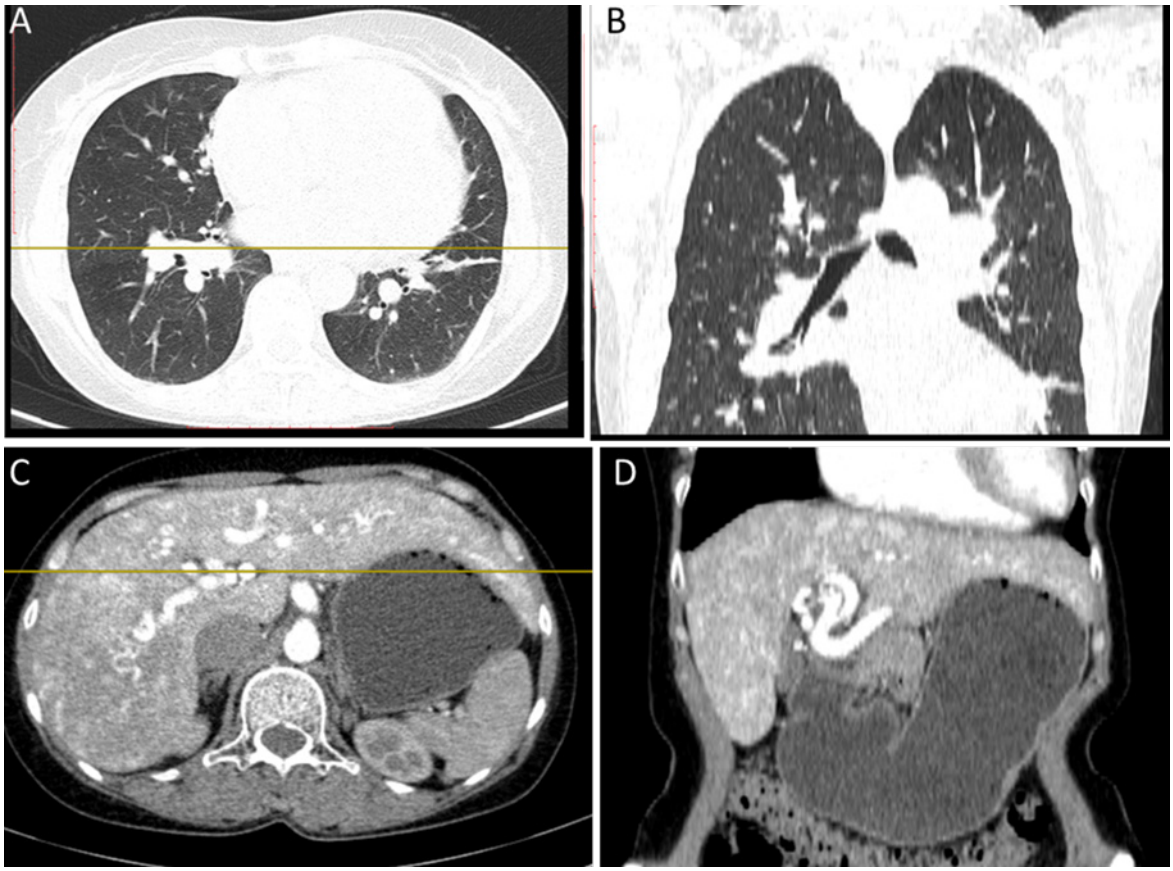

Figure 2. Vascular malformations in visceral organs. Chest CT lung window, axial or a coronal view. Pulmonary vessels are slightly dilated (A, B). Abdominal CT with contrast, axial or coronal view. The hepatic vessels are slightly dilated and curved (C, D)

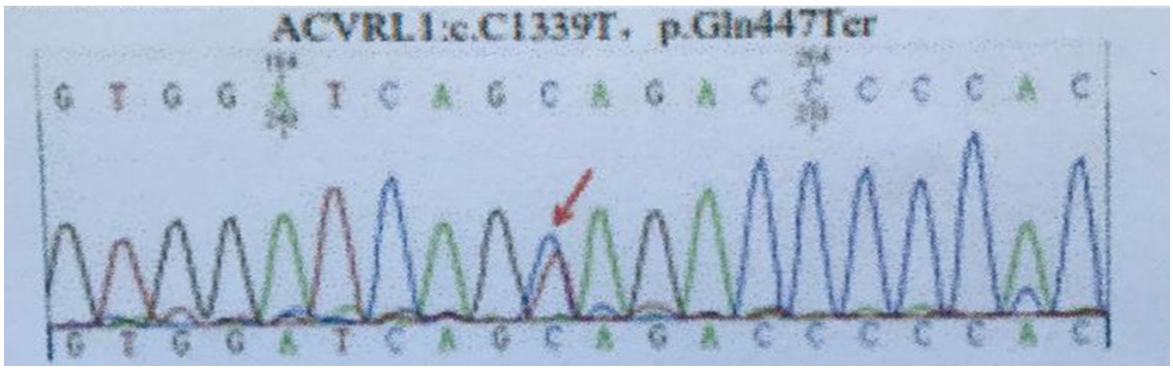

Figure 3. The Sequencing results of the ACVRL1 gene in the peripheral blood of patient with HH

enlargement of the liver, significantly dilated extrahepatic artery, early enhancement of hepatic veins, and early enhancement of the portal vein (Figure 2A, B). Also, dilatation of bilateral lobar pulmonary arteries (Figure 2C, D) were observed by enhanced axial and coronal CT images.

ACVRL1 gene mutation (5cC1339T; pGln447Ter) was detected. by genetic testing in the patient, which confirmed type 2 of ORWD.

She previously had experienced frequent episodes of epistaxis and does follow with an otolaryngologist. Recurrent nasal packing and electrocoagulation in heavy nasal bleeding caused septal perforation and deviation in the current case.

We suggested estrogen treatment for her. Since the initiation of estrogen treatment, the patient's episodes of epistaxis have been diminished. As for the mild hypochromic anemia, oral iron supplementation is recommended for the patient.

A detailed interview regarding repeated epistaxis and family history is necessary for the diagnosis of HHT. She gave birth to two daughters. There was no complication related to pregnancy and labor. Youngest daughter is 23 years old. A few telangiectasias were observed on her facial skin since the fall of 2018, but not epistaxis.

Discussion

The diagnosis of HTT is often delayed due to the rarity of the disease and the variety of clinical manifestations. Patients are often asymptomatic but usually experience dyspnea and tiredness which can occur due to anemia. The first clinical sign of HTT is epistaxis which occurs in more than 90% of patients older than 20 [3]. Anemia is most often the consequence of chronic gastrointestinal bleeding and in some cases of massive epistaxis. The reported patient presented to our clinic for evaluation of anemia and recurrent epistaxis. Her first epistaxis occurred around the age of 45 years and mild hypochromic microcytic anemia presented at the time of diagnosis.

The diagnosis of HHT is based on Curacao criteria [5,6]. All four Curacao criteria were observed in the current case: recurrent epistaxis, mucocutaneous telangiectasia, visceral lesions and family history. Besides mucocutaneous telangiectasias, AVMs mainly localize in the lung, liver, brain, and gastrointestinal tract (GIT) [1-3]. Therefore, screening for visceral AVMs is mandatory for HHT. In the present case, vascular malformations effects were found throughout the GIT: many telangiectasias were seen in oral mucous and upper GIT. CT scan demonstrated significantly dilated extra and intrahepatic arteries, early enhancement of hepatic veins, and also dilatation of bilateral lobar pulmonary arteries. Fortunately, cerebral AVMs were not detected in this case.

In 2009, an HHT working group recommended that patients who have 1 to 2 of Curacao criteria, should be tested most prevalent for ENG and ACVRL1. If the result is negative, SMAD4 should be considered (6). Five mutations in genes have been identified in HHT. About 90% of the cases are associated with heterozygous mutations of ENG and ACVRL1 genes, in the remaining 10% of HHT patients SMAD 4gene is affected [8-10,15]. ENG, ACVRL1, SMAD4 genes were screened in this case and ACVRL1 gene mutation (5cC1339T; pGln447Ter) was detected.

The ideal treatment for this disease is yet to be elucidated. HHT management includes systemic screening for visceral AVMs at regular intervals to reduce the risk of complications and symptomatic measures. Besides the management of epistaxis, we need more attention on the diagnoses and medical decisions made particularly in the case of epistaxis due to its complexity. We should follow her and her daughter for the future.

Conflict of Interest

The authors state no conflict of interest.

Acknowledgment

The authors provided no information regarding financial or institutional support or others who contributed to their study.

Reference

1. McDonald J, Bayrak-Toydemir P, Pyeritz RE. Hereditary hemorrhagic telangiectasia: an overview of diagnosis, management, and pathogenesis. Genet Med 2011; 13(7): 607–16.
2. Westermann CJ, Rosina AF, de Vries V, Coteau PAd. The prevalence and manifestations of hereditary hemorrhagic telangiectasia in the Afro-Caribbean population of the Netherlands Antilles: a family screening. Am J Med Genet 2003; 116(4): 324-28.
3. Assar OS, Friedman CM, White RI. The natural history of epistaxis in hereditary hemorrhagic telangiectasia. Laryngoscope 1991; 101: 977–80.
4. Plauchu H, Chadarévian D, Bideau A, Robert JM. Age-related clinical profile of hereditary hemorrhagic telangiectasia in an epidemiologically recruited population. Am J Med Genet 1989; 32(3): 291–7.
5. Shovlin CL, Guttmacher AE, Buscarini E, et al. Diagnostic criteria for hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). Am J Med Genet 2000; 91 (1): 66-7.

6. Faughnan ME, Palda VA, Garcia-Tsao G, et al. International guidelines for the diagnosis and management of hereditary haemorrhagic telangiectasia. Med Genet 2011; 48(2): 73-87.
7. Richards-Yutz J, Grant K, Chao EC, Walther SE, Ganguly A. Update on molecular diagnosis of hereditary hemorrhagic telangiectasia. Hum Genet 2010; 128(1): 61-77.
8. McAllister KA, Grogg KM, Johnson DW, Gallione CJ, Baldwin MA, et al. A TGF-beta binding protein of endothelial cells, is the gene for hereditary haemorrhagic telangiectasia type 1. Nat Genet 1994; 8(4): 345-51.
9. Johnson DW, Berg JN, Baldwin MA, et al. Mutations in the activin receptor-like kinase 1 gene in hereditary haemorrhagic telangiectasia type 2. Nat Genet 1996; 13: 189–95.
10. Gallione CJ, Repetto GM, Legius E, et al. A combined syndrome of juvenile polyposis and hereditary haemorrhagic telangiectasia associated with mutations in MADH4 (SMAD4). Lancet 2004; 363: 852–59.
11. Bayrak-Toydemir P, McDonald J, Markewitz B, et al. Genotype-phenotype correlation in hereditary hemorrhagic telangiectasia. Am J Med Genet 2006; 140: 463–70.
12. Letteboer TG, Mager JJ, Snijder RJ, et al. Genotype-phenotype relationship in hereditary haemorrhagic telangiectasia. J Med Genet 2006; 43: 371–77.
13. Gallione C, Aylsworth AS, Beis J, Berk T, Bernhardt B, et al. Overlapping spectra of SMAD4 mutations in juvenile polyposis (JP) and JP-HHT syndrome. Am J Med Genet 2010; 152A: 333–9.
14. Enkhjargal TS, Lkhagvasuren TS, Odgerel TS. Leaders in Medicine of Mongolia. XXX Scientist and Medical doctor Choijljaviin Tserenadmid, Ulaanbaatar, Munkhiin Useg 2018. p 25-7.
15. McDonald J, Damjanovich K, Millson A, Wooderchak W, Chibuk JM, et al. Molecular diagnosis in hereditary hemorrhagic telangiectasia: findings in a series tested simultaneously by sequencing and deletion/duplication analysis. Clin Genet 2011; 79(4): 335-44.